Hearing preservation surgery for neurofibromatosis Type 2–related vestibular schwannoma in pediatric patients

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Object. The authors reviewed the proportion of pediatric patients with neurofibromatosis Type 2 (NF2) in whom hearing was preserved after middle fossa resection of vestibular schwannoma (VS).

Methods. In this retrospective chart review the authors examined the cases of 35 children with NF2 who had undergone middle fossa resection (47 surgeries) between 1992 and 2004 in a neurotological tertiary care center. Surgical outcome was assessed using pure-tone average (PTA) thresholds obtained before and immediately after resection. Speech discrimination scores (SDSs) and pre- and postfacial nerve grades were also recorded. In 55% of surgeries, hearing of less than or equal to 70 dB PTA was maintained postoperatively. The American Academy of Otolaryngology–Head and Neck Surgery Class A hearing (PTA ≤ 30 dB and SDS ≥ 70%) was preserved in 47.7%. Facial nerve function was good (House–Brackmann Grades I or II) in 81% of the patients. Twelve patients had bilateral middle fossa resections; in nine (75%) of these patients hearing was maintained postoperatively in both ears.

Conclusions. More than half of the children with NF2 in the authors’ cohort experienced hearing preservation after middle fossa resection was performed for VS. The authors recommend this approach for preserving hearing in children with NF2.

KEY WORDS • neurofibromatosis Type 2 • vestibular schwannoma • middle fossa • hearing preservation • pediatric neurosurgery

The middle fossa approach was popularized by William House in 1961,15 and neurotologists have consistently refined this technique for lesions in the IAC and cerebellar pontine angle. This surgery was first performed to decompress the IAC in the presence of extensive otosclerosis of the labyrinthine bone. Although this approach was not useful for this indication, it paved the way for additional applications.3 Today, this surgery is more frequently undertaken in an attempt to preserve hearing when resecting VSs of 2 cm and smaller (in maximum diameter), both for unilateral VSs and for NF2-related VSs.4,12,20–23

Neurofibromatosis Type 2 is diagnosed by the criteria proposed by the National Institutes of Health in 1988:13 bilateral VSs, or a family history of NF2 plus a unilateral VS or at least two other NF2-related abnormalities. Patients commonly develop multiple schwannomas of the cranial, spinal, and peripheral nerves; meningiomas; ependymomas; optic gliomas; and posterior subcapsular lenticular opacities. Increased morbidity rates and early death may result due to these tumors’ anatomical location and growth characteristics despite the histologically benign nature of these tumors.10,16,19,25

Individuals with NF2 most commonly present with hearing loss. Other early symptoms of NF2 may include tinnitus and vestibular symptoms. The incidence of NF2 is estimated at one in 33,000 to 40,000 people and occurs in equal numbers across sex and ethnicity.11,19,25 Disease expression often occurs first when patients are in their late teens or early twenties.3,18

Advances in neuroimaging and genetic analysis have allowed early detection of VSs in persons with a known family history of NF2. We recommend that asymptomatic children of parents in whom NF2 was diagnosed undergo contrast-enhanced MR imaging of the entire head by 5 years of age. Otherwise, children of parents with NF2 who are younger than 5 years of age should undergo MR imaging as soon as symptoms are detected. Thin-slice (maximum 1 mm, 0 skip) Gd-enhanced MR imaging of the IAC is the definitive method of diagnosis and standard protocol for tumor follow up.5,17 Tumors that are 1 to 2 mm in diameter can now be detected on MR images before hearing has been significantly affected.7,11,21

Abbreviations used in this paper: AAO-HNS = American Academy of Otolaryngology–Head and Neck Surgery; IAC = internal auditory canal; MR = magnetic resonance; NF2 = neurofibromatosis Type 2; PTA = pure-tone average; SDS = speech discrimination score; VS = vestibular schwannoma.
Children without a family history of NF2 are frequently symptomatic to some degree and undergo MR imaging of the entire head as part of the diagnostic procedure. For example, one child in our sample experienced walking difficulties at an early age, and, subsequently, bilateral VSs were detected on the cranial MR image.

It has been our practice to attempt to preserve hearing in pediatric patients with NF2 because of their young age, knowing that these schwannomas will continue to grow over time. However, the actual proportion of children with NF2 who experience hearing preservation after middle fossa resection is unknown. It is possible that NF2-related VSs differ from unilateral VSs in undesirable ways for hearing preservation, perhaps particularly so in pediatric patients. It may be that the child will have a longer time with useful hearing without undergoing surgery than undergoing yet another major surgery.

In this retrospective chart review we examined hearing and facial nerve outcomes in children with NF2 undergoing middle fossa surgery for removal of VS, and we investigated the preoperative characteristics that may predict outcomes of postoperative hearing and facial nerve function.

Clinical Material and Methods

Patient Population

Between 1992 and October 2004, 35 children (<18 years of age) with NF2 underwent 47 middle fossa surgeries for VS resection at the House Clinic. All patients had documented NF2 on the basis of bilateral VSs seen on MR images, and they underwent planned surgery for VS removal. There were 17 boys (48%) and 18 girls (51%) in the cohort. Just more than half of the patients (18 [51%]) had a family history of NF2. The mean age at the time of surgery was 12.6 years (range 8–17 years). The mean tumor diameter in all procedures was 1.1 cm (range 0.40–3.2 cm). Most patients had good preoperative hearing (AAO-HNS Class A) before surgery (38 procedures [81%]). Patient demographics are shown in Table 1.

Twelve patients (34%; four boys and eight girls) had both VSs removed via the middle fossa approach in staged surgeries. If hearing preservation was accomplished on the first side and the second tumor required resection for hearing preservation, the patient and family were offered surgery on the contralateral side 6 months following surgery on the first side.

The main outcome variables in middle fossa VS resection are hearing preservation (measured by the four-frequency PTA and SDS) and facial nerve grade (assessed using the House–Brackmann scale). The AAO-HNS hearing classification for reporting outcome in hearing preservation was also used.

Surgical Procedure

Standardized information on the surgery and NF2-related symptoms were gathered from patients’ charts and surgeons’ reports. The preoperative facial nerve grade was evaluated at the presurgical visit, usually the day before the surgery. The postoperative facial nerve grade was evaluated on discharge from the hospital. All patients underwent audiography at least twice, once before surgery and again 2 weeks after surgery, to determine the level of hearing. Most patients also underwent audiography at a later point. Hearing preservation was defined as an immediate postoperative PTA of 70 dB or less. All patients with VS were asked to complete a 1-year postoperative questionnaire focusing on facial nerve and balance symptoms.

A standard operative form was completed at the time of surgery for variables associated with VS removal, including tumor origin, the nerves involved with the tumor, tumor adherence to normal-functioning nerves, the number of tumors found to be specifically associated with NF2, results of intraoperative monitoring, and any unusual findings that made the tumor removal unique. The surgical teams comprised a neurotologist and a neurosurgeon who both had extensive experience with NF2 and middle fossa craniotomies. The dictated surgical reports were quite consistent in their detail and content.

The degree of difficulty experienced when removing the tumor was categorized as routine, moderate, or difficult, based on surgical reports. Routine surgery was defined as little or no adherence of the tumor to the facial nerve or to the cochlear portion of the eighth cranial nerve. The procedure was categorized as moderate when developing the plane between the tumor and the facial and cochlear nerve was more complicated, but accomplished. A surgery reported as difficult indicated that the tumor was impacted in the IAC and was very involved with the facial and cochlear nerve. The number of nerves found to be involved during the surgery were also coded. Solitary tumors involving either portion of the vestibular nerve (superior or inferior) were coded as “1;” those involving both branches of the vestibular nerve (superior and inferior) were coded as “2;” and tumors involving both vestibular nerves and the cochlear nerve were coded as “3.” The difficulty rating of the surgery and the number of nerves involved were linearly combined to create a variable representing how demanding the surgery was, ranging from 2 to 6. A high number indicated a difficult surgery and a low number indicated a more routine surgery.

The severity of each patient’s NF2 disease was rated by counting the number of NF2-related symptoms. A patient could have a maximum of five NF2-related symptoms (bilateral VSs, additional cranial tumors [schwannomas and/or meningiomas], spinal tumors, eye abnormalities [epiretinal membranes and cataracts], and skin tumors). Therefore, the severity score could range from 1 to 5.

Statistical Analysis

Patient characteristics are presented descriptively and the

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**TABLE 1**

Demographics in 35 patients who underwent 47 surgeries for VSs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>age at op (yrs)</td>
<td>12.6 ± 2.3</td>
</tr>
<tr>
<td>tumor size (cm)</td>
<td>1.1 ± 0.63</td>
</tr>
<tr>
<td>preop PTA (dB)</td>
<td>14 ± 19</td>
</tr>
<tr>
<td>SDS (% correct)</td>
<td>95 ± 8.5</td>
</tr>
</tbody>
</table>

* Presented as the means ± standard deviations.
Hearing preservation in children with neurofibromatosis Type 2

predictors of postoperative PTA were assessed using linear regression (version 12.0, SPSS Inc.). Variables were considered to be predictors of hearing preservation if the regression coefficient was significant at the 0.05 level. Associations between categorical variables were assessed using the chi-square test, with significance set at a level of 0.05.

Results

Mean values are expressed as the means ± standard deviations. The cochlear nerve was intact at the end of each of the 47 procedures, and hearing was preserved after 26 surgeries (55%). Figure 1 depicts the individual postoperative PTA values for all surgeries. Overall, the mean postoperative PTA and SDS were 67 dB and 52% correct, respectively. Patients considered to have their hearing preserved had a mean PTA of 15.3 ± 14 dB and a mean SDS of 96 ± 7%. The AAO-HNS hearing classifications for pre- and postoperative hearing results are presented in Table 2. Fifty-six percent of the surgeries in patients with preoperative Class A hearing (very good hearing) were associated with preserved Class A hearing postoperatively.

The House–Brackmann facial nerve grade 1 year after surgery was normal or near normal (Grades I and II) after 38 (81%) of the 47 surgeries and was maintained at the preoperative grade or better in 77% (see Table 3). Fewer than half of the surgeries were recorded as routine, with the VSs arising from a single vestibular nerve (18 [38%]). The remainder of the surgeries were more complicated. Twelve surgeries (26%) were recorded as difficult, with tumors arising from both vestibular nerves and tumors that were adherent to the cochlear nerve.

The 35 patients exhibited a range of NF2-related symptoms, from multiple cranial, spinal, and eye tumors, and other schwannomas to bilateral VSs alone. Sixteen patients (46%) could be categorized as “mildly affected” and 19 (54%) as “severely affected.” The NF2 symptoms were modestly associated with family history. Patients with a family history of NF2 tended to be mildly affected more often than those without a family history of NF2 (65% compared with 22%).

Characteristics Related to Hearing Preservation

We hypothesized that the probability of hearing preservation was related to three classes of variables: disease-related (severity of NF2), patient-related (age at surgery, level of preoperative hearing), and surgery-related (difficult surgery). The multivariate statistical technique of discriminate analysis was used to determine which variable was most associated with preservation of hearing. The process of discriminate analysis maximizes the differences between two groups of patients (hearing preserved and hearing not preserved) using predetermined variables.

The analysis was conducted in two steps. First, the preoperative variables were analyzed to determine if information available before surgery would be of clinical use. In this analysis, severity and family history of NF2, age at surgery, tumor size, preoperative PTA; preoperative hearing thresholds of 250, 4000, and 6000 Hz; and preoperative speech discrimination were reviewed to determine the clusters of variables most associated with preservation of serviceable hearing. Table 4 shows the comparison of these factors between those with and those without preserved hearing. The discriminate analysis correctly predicted the hearing outcome of surgery for 77% of the 47 cases, indicating that the variables discriminated very well between the two groups. The severity of NF2 was the strongest discriminator of hearing outcome, with fewer symptoms associated with hearing preservation. Smaller VS size, better preoperative hearing, younger age at surgery, and a family history of NF2 were also significantly associated with hearing preservation.

The second discriminate analysis was performed to add the surgical difficulty variable to the preoperative variables to determine if there was an added ability to discriminate between the hearing preservation groups. Surgical difficulty became the best predictor of hearing outcome. Thus, the

![Fig. 1. Graph showing the individual postoperative PTAs (47 surgeries). The horizontal line indicates preserved hearing.](image)

**TABLE 2**

<table>
<thead>
<tr>
<th>Preop Class</th>
<th>Postop Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (39 ops)</td>
<td>B 22</td>
</tr>
<tr>
<td>B (1 op)</td>
<td>C 0</td>
</tr>
<tr>
<td>C (5 ops)</td>
<td>D 0</td>
</tr>
</tbody>
</table>

* The preoperative SDS was not available in two patients. The scores are based on the AAO-HNS classification (Class A, PTA ≤ 30 dB and SDS ≥ 70%; Class B, PTA > 30 dB and ≤ 50 dB and SDS ≥ 50% or PTA ≤ 30 dB and SDS ≤ 50% and < 70%; Class C, PTA > 50 dB and SDS ≥ 50%; and Class D, PTA any level and SDS < 50%.

**TABLE 3**

<table>
<thead>
<tr>
<th>Preop Grade</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>VI</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (43 ops)</td>
<td>33</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>II (3 ops)</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>III (1 op)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Grade I denotes normal function and Grade VI, paresis.
fewer adhesions the tumor had to surrounding nerves and the fewer nerves involved with the tumor, the better the chance of hearing preservation. The second discriminate analysis correctly predicted 93% of the 47 cases, confirming the hypothesis that the conditions associated with the location of the schwannoma discovered during surgery significantly impacts hearing outcome. Figure 2 illustrates these differences in hearing outcome by NF2 severity and surgical difficulty. The preoperative variables also contributed to the significant discrimination between the hearing outcome groups as described in the first analysis. Table 5 summarizes the factors predictive of hearing preservation.

**Bilateral Middle Cranial Fossa Resection**

A subsample of the 12 patients underwent bilateral surgery following successful preservation of hearing on the first side. Three (25%) of these patients lost hearing on the second side, and the remaining nine (75%) had hearing preserved on both sides. Ten (83%) of these patients had bilateral facial nerve Grade I or II postoperatively. Given that the level of surgical difficulty was a major predictor of hearing preservation in the overall sample, we examined the association between left- and right-sided ratings of how demanding the surgery was in the patients who underwent bilateral surgery. The level surgical difficulty performed on the left and right side was equal (not significant, chi-square test).

**Follow Up of Long-Term Hearing**

Patients involved in four of the 26 procedures resulting in hearing preservation were lost to long-term follow up. Five sides (22%) worsened (PTA increase > 10 dB) over an average of 6 years in cases monitored by long-term audiography. There were no intervening hearing tests to determine more accurately the duration of time with good hearing in these five cases. The remaining sides with hearing preservation (78%) retained good hearing (PTA did not increase) at an average follow-up period of 2.8 years, with one patient retaining hearing for more than 7 years.

**Discussion**

Children with NF2 are vulnerable to loss of sensory function, particularly if they experience ophthalmological symptoms. The ability to preserve hearing in these patients would be of great clinical benefit and would outweigh the risks involved in major surgery. To determine clinical benefit, we assessed the proportion of patients who experienced hearing preservation and facial nerve function preservation postoperatively. In addition, we assessed the relationship between patient and surgery characteristics and hearing preservation in an attempt to understand the factors associated with preserved hearing. A total of 35 patients were included in this study, and of those 12 underwent bilateral middle fossa removal of a VS.

Hearing was preserved to 70 dB or less in 55% of the 47 surgeries and was bilaterally preserved in 75% of the patients undergoing bilateral surgeries. For those in whom hearing was preserved, the mean PTA was 15.3 dB, with a mean SDS of 96%. Good hearing was maintained up to an average of 2.8 years in 78% of those procedures that resulted in preserved hearing. Some sides showed progressive loss of hearing at an average of 6 years. However, it is not known whether this was due to the disease or as a result of the procedure.

The preoperative facial nerve grade was preserved in 77% of the surgeries and was excellent (Grade I or II) in 81% of the surgeries. Clearly, there is a clinical benefit to attempt hearing preservation surgery for VSs in children with NF2. Both hearing and facial function were preserved in a high proportion of patients.

The results of the discriminate analyses provided a clinical picture of the type of candidates for NF2 surgery who are most likely to retain hearing: those who are younger, have normal or near-normal hearing, have a family history of NF2, and who are not experiencing other severe NF2-

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**TABLE 4**

*Discriminant analysis results: hearing preservation surgery predictors by procedures with hearing preserved or not preserved*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hearing Preserved (26 cases)</th>
<th>Hearing Not Preserved (21 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>age at op (yrs)</td>
<td>12.0 ± 2.0</td>
<td>15.3 ± 2.5</td>
</tr>
<tr>
<td>tumor size (cm)</td>
<td>0.9 ± 0.5</td>
<td>1.5 ± 0.6</td>
</tr>
<tr>
<td>preop PTA (dB)</td>
<td>7 ± 13</td>
<td>22 ± 22</td>
</tr>
<tr>
<td>SDS (% correct)</td>
<td>98 ± 7</td>
<td>93 ± 11</td>
</tr>
<tr>
<td>family history of NF2 (%)</td>
<td>65</td>
<td>43</td>
</tr>
<tr>
<td>severity of NF2 symptoms</td>
<td>median = routine op</td>
<td>median = more difficult op</td>
</tr>
</tbody>
</table>

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**TABLE 5**

*List of factors associated with hearing preservation in children with NF2*

<table>
<thead>
<tr>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>routine, less difficult op</td>
</tr>
<tr>
<td>fewer NF2-related symptoms</td>
</tr>
<tr>
<td>smaller tumor size at op</td>
</tr>
<tr>
<td>better hearing</td>
</tr>
<tr>
<td>younger age at op</td>
</tr>
<tr>
<td>family history of NF2</td>
</tr>
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</table>
related symptoms. It is very important that the physician obtain a complete history of the patient to determine the severity of NF2. A whole-systems approach to obtaining the disease history and severity is necessary, including information about tumors in the spine, other intracranial tumors, ophthalmological symptoms, and skin tumors. The number of previous surgeries related to NF2 also indicates the severity of the disease.

In addition to the information available preoperatively, circumstances encountered during the surgery significantly impacted hearing outcome. If the schwannoma was very adherent to the facial and cochlear nerve, or if there were numerous small tumors within the cerebellopontine angle, the chance of hearing preservation was lower. In the future, researchers will be challenged to develop methods of assessing these variables before surgery. For example, advancements in imaging techniques may provide clearer images of the number of tumors in the cerebellopontine angle. Currently, imaging researchers are engaged in developing better methods with high-resolution MR imaging for visualizing intracranial structures.

It was instructive that, in cases of bilateral surgery, the level of difficulty encountered in one ear was not associated with the difficulty in the other. That is, surgical difficulties were local to each ear. These results suggest that although knowledge of the impact of NF2 on the patient is an important prognostic indicator, the surgeon’s expertise and tumor-specific characteristics are significant variables affecting outcome.

Magnetic resonance imaging of the IAC just before surgery (within 1 month of surgery) can be of great benefit to the surgeon regarding location and number of tumors. For example, in the NF2 Natural History study, we required thin-slice images (1 mm, 0 skip) to be obtained through the IAC for good tumor visualization. We recommend this acquisition protocol for preoperative studies of children with NF2.

The level of facial function preservation in children with NF2 was very good (similar to that in adults who underwent unilateral middle fossa surgery). Preservation of facial function is critical in pediatric patients for obvious social interaction and quality of life reasons. Young patients facing a chronic disease would be better able to cope without the additional difficulties of facial dysfunction. These results confirm and extend our previous findings regarding hearing preservation surgery in which the middle fossa approaches were used. Here, in a greater percentage of patients a Class A hearing level (47%) was preserved relative to a large sample of patients with unilateral VS (33% [five patients]). In the earliest study the authors did not observe a relationship between preoperative hearing and outcome. However, they examined speech discrimination ability only; here we examined PTA thresholds as well as speech discrimination. Better preoperative hearing was related to better postoperative hearing, confirming findings from our previous study.

Younger patients with smaller tumors tended to be better candidates for hearing preservation. In addition, the difference in average tumor size between the groups in which hearing was preserved was just 0.6 cm, and this small amount was statistically significant. Taken together, these results would suggest that middle fossa surgery is better when attempted sooner rather than later in the disease course, even when hearing is good. This result is important for parents considering the time course to various surgeries or other interventions for their child’s NF2 symptoms. At this time, however, evidence for alternative interventions, such as radiosurgery, has not been described in the literature for children with NF2.

Conclusions

It is our practice to perform middle fossa resection in children with NF2, and the sooner in the disease process, the better. Our results indicate that hearing and facial nerve function can be successfully preserved using this approach. Factors to consider include patient age, severity of additional NF2-related symptoms, and obtaining high-quality, thin-slice MR images before surgery. Bilateral middle fossa resection following hearing preservation on the first side is also successful and potentially preserves hearing in both ears.

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References


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